Honey Badger Don’t Care!

So why don’t honey badgers care about venoms that can kill almost any other animal?

Danielle Drabeck, a University of Minnesota grad student, wanted to study this question on a molecular level, but she ran into a problem: Honey badgers aren't found in Minnesota or even the Western Hemisphere, but only in **Africa, the Middle East, and India**.

“The hardest part, honest to God, was finding honey badger tissue” to study, says Drabeck—which likely explains why no other biologists ever investigated how honey badgers resist cobra venom. Working with biologist **Sharon Jansa** and biochemist **Antony Dean**, Drabeck obtained some precious honey badger blood from the zoos of San Diego and Fort Wayne, Indiana.

With this blood, the scientists **figured out, for the first time, how the honey badger defends itself on the molecular level against its venomous prey**. The blood also revealed clues of an evolutionary arms race. And it might help us design better antivenoms for humans bitten by venomous snakes.

But why would a honey badger need venom resistance in the first place? Why doesn’t it avoid venomous snakes, like more sensible mammals?

“Snakes,” says Drabeck, “are an excellent source of meat.” Up to 25 percent of the honey badger’s omnivorous diet consists of venomous snakes. But the honey badger doesn’t eat snakes out of desperation. Evolving to withstand snake venom is like being the only person at a party who can eat the extra-hot salsa: You get it all to yourself. Plus, Drabeck says, this means the honey badger gets to hunt fairly slow-moving prey with only one pointy end, rather than fast prey with one pointy end plus four sets of claws.

But it’s one hell of a pointy end. Venom has more than 100 proteins and other molecules that could potentially poison a snake’s victim—meaning that honey badgers need multiple defenses. To narrow the field, Drabeck guessed that the honey badger had probably evolved a defense similar to that used by other venom-resistant critters like mongooses. She focused on a defense against a nasty class of molecules in cobra venom called alpha-neurotoxins that paralyze the muscles used for breathing. These neurotoxins essentially park in a muscle cell’s nicotinic acetylcholine receptor, preventing the cell from receiving the nervous system’s signals to keep working.

Drabeck figured that the receptor targeted by cobra neurotoxin had probably changed to prevent the neurotoxin from parking there. Once she had the blood from the zoos’ honey badgers, Drabeck extracted DNA and sequenced part of the gene that contains the blueprint for making the receptor. Drabeck discovered several mutations in that gene that tweak the receptor. Cobra neurotoxin fits as well in the tweaked receptor as an SUV in a compact’s parking spot—and therefore it can’t paralyze the honey badger’s breathing.

Drabeck wasn’t surprised by these mutations, but she was surprised when she compared the honey badger’s tweaks to those found in other mammals. These tweaks had evolved independently in at least four species: honey badgers, mongooses, hedgehogs, and pigs. The hedgehog—which loves to eat venomous snakes—wasn’t a surprise. But the pig? “We were pretty excited by that,” says Drabeck. She hadn’t expected pigs to have molecular defenses against venom; biologists knew wild pigs could survive snakebites but assumed that was because their thick skin and fat acts like armor against fangs. But wild pigs, like honey badgers, have long shared the same parts of the world as venomous snakes—giving them an incentive to evolve venom resistance. And that in turn has given the snakes an incentive to evolve more toxic venom.

Venomous snakes and resistant honey badgers, it turns out, are locked in what Jansa describes as a “tit-for-tat arms race.” This co-evolution is an unending cycle of one-upmanship between predators and prey. When venomous snakes are attacked by venom-resistant honey badgers, the snakes need to evolve more toxic venom to protect themselves.